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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/787,421	02/26/2004	Majed M. Hamawy	960296.99187	5432

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EXAMINER	
ROONEY, NORA MAUREEN	
ART UNIT	PAPER NUMBER
1644	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/20/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/787,421	HAMAWY, MAJED M.	
	Examiner	Art Unit	
	Nora M. Rooney	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 January 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4-9 and 12-16* is/are pending in the application.

4a) Of the above claim(s) *14-16* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-2, 4-9 and 12-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

RESPONSE TO APPLICANT'S AMENDMENT

1. Applicant's amendment filed on 01/24/2007 is acknowledged.

2. Claims 1-2, 4-9 and 12-16 are pending.

3. Claims 14-16 stand withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to nonelected inventions.

4. Claims 1-2, 4-9 and 12-13 are under examination as they read on a method of monitoring whether an animal is experiencing a disease involving smooth muscle cell abnormalities wherein the disease is transplant rejection.

5. The following new grounds of rejection are necessitated by the amendment submitted on 01/24/2007.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1-2, 3-9 and 12-13 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a New Matter rejection.

8. The phrase "kidney disease" claimed in claim 1, line 3 represents a departure from the specification and the claims as originally filed.

Applicant's claims filed on 02/26/2004 do not point to the specification for support for the newly added limitation "kidney disease". The specification and the claims as originally filed do not provide a clear support of "kidney disease."

9. The phrase "or materials derived therefrom" claimed in claim 1, line 22 and claim 6, line 22 represents a departure from the specification and the claims as originally filed.

Applicant's claims filed on 02/26/2004 do not point to the specification for support for the newly added limitation "or materials derived therefrom." The specification and the claims as originally filed do not provide a clear support of "or materials derived therefrom."

10. The phrases "a means of perceiving the marker protein" and "marker protein so perceived" claimed in claim 1, lines 23 and 25-26 and claim 6, lines 23 and 25-26 represent a departure from the specification and the claims as originally filed.

Applicant's claims filed on 02/26/2004 do not point to the specification for support for the newly added limitations of "a means of perceiving the marker protein" and "marker protein so perceived." The specification and the claims as originally filed do not provide a clear support of "a means of perceiving the marker protein" and "marker protein so perceived."

11. The phrase "attempting to visualize the marker protein" claimed in claim 1, line 28 and claim 6, line 28 represents a departure from the specification and the claims as originally filed.

Applicant's claims filed on 02/26/2004 do not point to the specification for support for the newly added limitations of "attempting to visualize the marker protein." The specification and the claims as originally filed do not provide a clear support of "attempting to visualize the marker protein."

12. Claims 1-2, 3-9 and 12-13 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for: a method of monitoring whether an animal, including a primate, has kidney transplant rejection comprising analyzing a kidney sample taken from the animal for the presence of the protein of SEQ ID NO;1 using antibodies to SEQ ID NO:1, does not reasonably provide enablement for: a method of monitoring whether an animal that has received a transplanted kidney has kidney disease involving smooth muscle cell abnormalities, the method comprising: analyzing **a sample** taken from the animal for the presence of a marker protein selected from the group consisting of: (a) phosphorylated protein having a sequence of

SEQ. ID NO. 1 in a form comprising phosphorylated tyrosine; (b) phosphorylated protein having a sequence of SEQ. ID NO. 2 in a form comprising phosphorylated tyrosine; (c) protein having a sequence of SEQ. ID NO. 1; and (d) protein having a sequence of SEQ. ID NO. 2, wherein the disease is kidney transplant rejection; an wherein the analyzing comprises: contacting **the sample or materials derived therefrom** with a **means of perceiving the marker protein**; an either: (i) comparing the amount of marker protein so perceived with the amount of marker protein in a known standard to diagnose whether the animal has such a disease; or (ii) **attempting to visualize the marker protein** to diagnose whether the animal has such a disease of claim 1; wherein the animal is a primate of claim 2; wherein the method further comprises examining **protein fragments** solubilized from a homogenate of the sample for the presence of **a fragment of the selected marker protein** of claim 4; wherein the marker protein is SEQ. ID NO. 1 in a form in which at least a tyrosine of SEQ. ID NO. 1 has been phosphorylated of claim 5; A method of monitoring whether a transplanted kidney is being rejected by an animal recipient of the transplant; comprising: analyzing **a sample** taken from the recipient for the degree of presence of a marker protein selected from the group consisting of: (a) phosphorylated protein having a sequence of SEQ. ID NO. 1 in a form comprising phosphorylated tyrosine; (b) phosphorylated protein having a sequence of SEQ. ID NO. 2 in a form comprising phosphorylated tyrosine; (c) proteins having a sequence of SEQ. ID NO. 1; and (d) protein having a sequence of SEQ. ID NO. 2; wherein the analyzing comprises: contacting **the sample or materials derived therefrom** with a **means of perceiving the marker protein**; and either: (i) comparing the amount of marker protein so perceived with the amount of marker protein in a known standard to diagnose whether the animal has such a disease; or (ii) **attempting to**

visualize the marker protein to diagnose whether the animal has such a disease of claim 6; wherein the method comprises examining protein fragments solubilized from a homogenate of the sample for the presence of **a fragment of the selected marker protein** of claim 7; wherein the animal is a primate of claim 8; wherein the animal is a human of claim 9; wherein the sample is a portion of a transplanted kidney of claim 12; wherein the marker protein is SEQ. ID NO. 1 in a form in which at least a tyrosine of SEQ. ID NO. 1 has been phosphorylated of claim 13 for the same reasons as set forth in the previous Office Action mailed on 12/28/2006.

Further, on pages 7-20 of the specification a method is disclosed for analyzing kidney tissue samples for the phosphorylated protein of SEQ ID NO:1 to determine kidney transplant rejection status. Experiments were performed by immunoblot using of anti-phosphotyrosine antibody after SDS-PAGE 2 D gel electrophoresis, polyacrylamide electrophoresis, mass spectrometry, immunohistochemistry, light microscopy and RT-PCR from kidney tissue samples of mice, rhesus monkeys, baboons and rats.

Applicant has not disclosed "a means of perceiving the marker protein" as recited in claims 1 and 6. One of ordinary skill in the art would not be able to determine what "means" are encompassed by this claim recitation. It is especially unclear which of the "means" encompassed by the claim recitation would actually work in the claimed invention. Therefore, it would require an undue amount of experimentation to practice the invention within the scope of the claims.

Claims 4 and 7 recite examining protein fragments for the presence of a fragment of the homogenate of the sample to monitor kidney transplant rejection status. However, the

specification does not disclose any structure for the protein fragments. There is a lack of direction and guidance as to which fragments would effectively monitor kidney transplantation status in the claimed invention. There is also a lack of guidance given as to the significance of amino acid differences at given positions within the protein, though the importance of homology at certain positions is well known the art. The claims encompass many proteins that would not work. Therefore, an undue amount of experimentation is required to enable one of skill in the art to practice the claimed invention.

The specification does not disclose "attempting to visualize the marker protein" as recited in claims 1 and 6. One of ordinary skill in the art would not be able to determine what the claim recitation "attempting to visualize" means. It is especially unclear how "attempting to visualize the marker protein", as encompassed by the claim recitation, would actually be done in the claimed invention. For example, one could attempt to "visualize" the unmarked SBP-1 by examining tissue with their eyes, though that would clearly not work in the claimed invention. The claim recitation is very broad and is not supported by the specification's disclosure. Therefore, it would require an undue amount of experimentation to practice the invention within the scope of the claims.

The specification does not provide sufficient support for the any "sample" to diagnose kidney transplant rejection as recited in claims and 6 and the claims dependent thereupon. The specification only provides support for a tissue sample from an animal's kidney. A bone sample would not be useful in the claimed invention, though it is encompassed by the claims. Applicant

has not disclosed the presence or absence of phosphorylated or unphosphorylated SBP-1 or SBP-2 in any normal samples but kidney. Therefore, the disclosure in the specification does not support that a decrease of SBP-1 or SBP-2 in any sample, including urine, has any correlation with a smooth muscle abnormality or kidney transplant rejection.

In addition, claims 1 and 6 and those dependent thereupon recite "a sample or materials derived therefrom" to monitor kidney transplant rejection status. These terms recite no structure for the sample. There is a lack of direction and guidance as to which samples and sample fractions or derivatives would effectively monitor kidney transplantation status in the claimed invention. Therefore, an undue amount of experimentation is required to enable one of skill in the art to practice the claimed invention.

The specification does not provide support for monitoring disease with: the protein of SEQ ID NO:2 as recited in parts b and d of claims 1 and 6; or the fragments of SEQ ID NO:1 or SEQ ID NO:2 as recited in claims 4 and 7. It is unclear whether the presence of the un-phosphorylated and/or phosphorylated protein of SEQ ID NO:2 or fragments of SEQ ID NO:1 or SEQ ID NO:2 correlates with transplant rejection status.

The specification disclosure does not enable one skilled in the art to practice the invention without an undue amount of experimentation.

Applicant's arguments filed on 01/24/2007 have been fully considered, but are not found persuasive.

Applicant argues that the claims have been amended to over come the enablement rejections regarding percent homology and fragment molecular molecular weight. Applicant also argues that the applicants have confirmed that unphosphorylated SBP-1 is a useful marker for monitoring kidney transplantation rejection in a post-filing reference. Applicant argues that this was projected in the application.

However, neither the specification nor the post-filing reference supports the use of unphosphorylated or phosphorylated SEQ ID NO:2 to diagnose kidney transplantation status. As stated in the previous office action, the art acknowledges that function cannot be predicted based solely on structural similarity to a protein found in the sequence databases and recognized that it was unpredictable if any functional activity will be shared by two polypeptides having less than 100% identity over the full length of their sequences. Attwood (Science 2000; 290:471-473) teaches that "[i]t is presumptuous to make functional assignments merely on the basis of some degree of similarity between sequences. Similarly, Skolnick et al. (Trends in Biotech. 2000; 18(1):34-39) teach that the skilled artisan is well aware that assigning functional activities for any particular protein or protein family based upon sequence homology is inaccurate, in part because of the multifunctional nature of proteins (e.g., "Abstract" and "Sequence-based approaches to function prediction", page 34). Even in situations where there is some confidence of a similar overall structure between two proteins, only experimental research can confirm the

artisan's best guess as to the function of the structurally related protein (see in particular "Abstract" and Box 2). Therefore, at the time the invention was made, the applicant did not sufficiently describe the invention such that one of ordinary skill in the art could practice the invention without undue experimentation.

13. Claims 1-2, 3-9 and 12-13 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention for the same reasons as set forth in the previous Office Action mailed on 12/28/2006.

Applicant is in possession of: a method of monitoring whether an animal, including a primate, has kidney transplant rejection comprising analyzing a kidney sample taken from the animal for the presence of the protein of SEQ ID NO;1 using antibodies to SEQ ID NO:1.

Applicant is not in possession of: a method of monitoring whether an animal that has received a transplanted kidney has kidney disease involving smooth muscle cell abnormalities, the method comprising: analyzing a sample taken from the animal for the presence of a marker protein selected from the group consisting of: (a) phosphorylated protein having a sequence of SEQ. ID NO. 1 in a form comprising phosphorylated tyrosine; (b) phosphorylated protein having a sequence of SEQ. ID NO. 2 in a form comprising phosphorylated tyrosine; (c) protein having a

sequence of SEQ. ID NO. 1; and (d) protein having a sequence of SEQ. ID NO. 2, wherein the disease is kidney transplant rejection; an wherein the analyzing comprises: contacting the sample or materials derived therefrom with a **means of perceiving the marker protein**; an either: (i) comparing the amount of marker protein so perceived with the amount of marker protein in a known standard to diagnose whether the animal has such a disease; or (ii) attempting to visualize the marker protein to diagnose whether the animal has such a disease of claim 1; wherein the method further comprises examining **protein fragments** solubilized from a homogenate of the sample for the presence of a fragment of the selected marker protein of claim 4; A method of monitoring whether a transplanted kidney is being rejected by an animal recipient of the transplant, comprising: analyzing a sample taken from the recipient for the degree of presence of a marker protein selected from the group consisting of: (a) phosphorylated protein having a sequence of SEQ. ID NO. 1 in a form comprising phosphorylated tyrosine; (b) phosphorylated protein having a sequence of SEQ. ID NO. 2 in a form comprising phosphorylated tyrosine; (c) proteins having a sequence of SEQ. ID NO. 1; and (d) protein having a sequence of SEQ. ID NO. 2; wherein the analyzing comprises: contacting **the sample or materials derived therefrom** with a **means of perceiving the marker protein**; and either: (i) comparing the amount of marker protein so perceived with the amount of marker protein in a known standard to diagnose whether the animal has such a disease; or (ii) attempting to visualize the marker protein to diagnose whether the animal has such a disease of claim 6; and wherein the method comprises examining protein fragments solubilized from a homogenate of the sample for the presence of **a fragment of the selected marker protein** of claim 7.

Further, claims 4 and 7 recite examining protein fragments for the presence of a fragment of the homogenate of the sample to monitor kidney transplant rejection status. However, the specification does not disclose any structure for the protein fragments.

Claims 1 and 6 and those dependent thereupon recite "a sample or materials derived therefrom" to monitor kidney transplant rejection status. These terms recite no structure for the sample.

Applicant has not disclosed in the specification any "means of perceiving the marker protein." This term is very broad and covers "means" that are as diverse as antibodies, functional activity assays and microscopes. There is no support in the specification for analyzing the proteins by any means.

Therefore, the skilled artisan cannot envision all of the contemplated analysis reagent/procedure possibilities recited in the instant claims. Consequently, conception cannot be achieved until a representative description of the structural and functional properties of the claimed invention has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC1993). The Guidelines for the Examination of Patent Application Under the 35 U.S.C.112, ¶ 1"Written Description" Requirement make clear that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species disclosure of relevant, identifying

characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 20001, see especially page 1106 3rd column).

Applicant has disclosed and reduced to practice detection of a single protein species, SEQ ID NO:1 using antibodies to the protein for monitoring kidney transplantation status.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Applicant is directed to the final Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Applicant's arguments filed on 01/24/2006 have been fully considered, but are not found persuasive.

Applicant argues that the written description concerns have been addressed by amendment.

However, the claims still recite using protein fragments to diagnose kidney transplant rejection. As stated in the previous Office Action mailed on 12/28/2006, applicant has disclosed only proteins consisting of SEQ ID NO:1 and 2 for monitoring kidney transplant rejection status; therefore, the skilled artisan cannot envision all the contemplated protein possibilities recited in the instant claims. Applicant has disclosed and reduced to practice a single protein species, SEQ ID NO:1 for monitoring kidney transplantation status. The genus of all protein fragments that are encompassed by the instant claims has a great deal of variability and includes all as yet undiscovered protein fragments. Applicant has not disclosed, nor does the art recognize, the requisite structural features of the encoded polypeptides which results in the disclosed functional activities of being able to be used to monitor kidney transplantation status, a feature deemed essential to the instant invention. Therefore, one of skill in the art would not recognize Applicant to be in possession of the genus of all protein fragments encompassed by the instant claims.

14. In view of the amendment filed on 01/24/2007, only the following rejections are maintained.

15. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

16. Claims 1-2, 4-9 and 12-13 stand rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted step is a correlation/ resolution step: it is unclear how to determine the kidney transplant rejection status by analyzing the protein of SEQ ID NO:1 or 2. The minimum requirements for method steps minimally include a contacting step in which the reaction of the sample with the reagents necessary for the assay is recited, a detection step in which the reaction steps are quantified or visualized, and a correlation step describing how the results of the assay allow for the determination.

Applicant's arguments filed on 01/24/2007 have been fully considered, but are not found persuasive.

Applicant argues that the claims have now been made clearer that the analyzing step involves contacting the sample, or something derived from it such as a homogenate, to facilitate perceiving the presence of the marker, followed by a comparison to a known standard or visualization.

However, claims 1-2, 4-9 and 12-13 remain indefinite because it is unclear whether an increase or a decrease (presence vs absence) of SEQ ID NO:1, SEQ ID NO:2, phosphorylated SEQ ID NO:1 **and** phosphorylated SEQ ID NO:2 correlates with disease. It is suggested that applicant amend the claims to

recite language that indicates the presence, absence or amount (decreased or increased) of protein compared to a standard correlates with disease.

17. No claim is allowed.

18. Applicant's amendment necessitated the new grounds of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nora M. Rooney whose telephone number is (571) 272-9937. The examiner can normally be reached Monday through Friday from 8:30 am to 5:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571)

272-0841. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

April 12, 2007

Nora M. Rooney, M.S., J.D.

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Maher M. Haddad

MAHER M. HADDAD
PRIMARY EXAMINER